

Mild impairment of neuro-otological function in early treated congenital hypothyroidism

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Abstract

Pure tone audiometry, tympanometry, acoustic stapedial reflex thresholds (ASRTs), and auditory evoked brain stem responses (AEBRs) were carried out in 38 children with early treated congenital hypothyroidism aged 10–12 years, together with tests of vestibular function (electronystaggraphy, rotational, and caloric tests). Sensorineural hearing loss with thresholds of greater than 15 dB was detected in 18 children (10 at 8 kHz only); only two children had more than 40 dB hearing loss, each in one ear. Raised ASRTs were found in eight children and two children had abnormal AEBRs. Of the 29 children tested, 12 had an abnormality of vestibular function. Although not significant at the 5% level, there was a tendency for the abnormalities to be more prevalent and severe in the children with more severe hypothyroidism, as judged by pretreatment plasma thyroxine. It is concluded that (i) mild abnormality of hearing is still common in children with congenital hypothyroidism despite early treatment but this is much less severe than that found before neonatal screening and (ii) mild abnormalities of vestibular function may be common in early treated congenital hypothyroidism.

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It has long been recognised that congenital hypothyroidism can be associated with hearing impairment. Early studies concentrated on endemic hypothyroidism caused by low iodine intake and Pendred's syndrome, a rare recessively inherited condition in which a defect in thyroid hormone biosynthesis is associated with hearing loss and the Mondini-type deformity of the cochlea. A few studies have been carried out on children with sporadic congenital hypothyroidism born before widespread introduction of neonatal screening and these have shown severe bilateral impairment of hearing in 20–36% of cases.^{1–3} We are aware of only two studies in early treated congenital hypothyroidism,^{4,5} both of which showed increased prevalence of mildly impaired hearing. Similarly, there is little information on vestibular function in sporadic congenital hypothyroidism, apart from that published by Sato *et al* showing abnormal vestibular function in 10 out of 13 subjects with late treated congenital hypothyroidism.⁶

The present study was carried out to record the prevalence of audiovestibular problems in a cohort of children born in 1978–81 with early treated congenital hypothyroidism diagnosed by screening. Hearing was assessed by pure tone audiometry, together with measurements of acoustic stapedial reflex thresholds (ASRTs), and auditory evoked brain stem responses (AEBRs). Vestibular function was studied by carrying out electronystagmography (ENG), vestibular ocular reflex testing, and caloric testing. In this paper we describe our findings which indicate that mild impairment of hearing and vestibular function may still occur in children with congenital hypothyroidism despite early diagnosis and treatment.

Patients and methods

PATIENTS

The nine boys and 29 girls who agreed to participate in this study and who had tests of neuro-otological function between the ages of 10 and 12 years are members of a larger cohort of children with congenital hypothyroidism born in 1978–81 who have been followed up to the age of 10 years.^{7–9} The sex distribution, severity of hypothyroidism (judged by median pretreatment plasma thyroxine (40 nmol/l), and thyroid stimulating hormone (292 mU/l)), as well as median age at start of treatment (28 days) were similar in the children who were tested and the 40 other members of the cohort who did not participate in the study.

Tests were carried out over a period of three years, using the same equipment. The procedures were lengthy and demanding and only 29 children were able to complete every component of all the tests; details of patient numbers for each test are given in tables 1 and 2. The study was approved by the local ethics committee and families were given a written description of the test procedures, followed by further verbal explanations when necessary.

METHODS

Clinical assessment

Tests at the start of the examination included otoscopy, gait assessment with Unterberger and heel/toe walking tests, eye patch cover tests to uncover latent strabismus, and examination for spontaneous nystagmus, pursuit, and saccade eye movements.

Audiological assessment

The following procedures were carried out to assess hearing.

(A) *Pure tone audiometry* using a Kamplex

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Table 1 Number (%) of normal and abnormal hearing tests in 76 ears tested in 38 children with congenital hypothyroidism. The results are grouped by severity of hypothyroidism (severe: pretreatment plasma thyroxine 40 nmol/l or below; less severe; pretreatment plasma thyroxine over 40 nmol/l)

	Children with congenital hypothyroidism		
	Severe (n=42)	Less severe (n=34)	Total (n=76)
(A) No of ears tested			
Normal hearing: threshold 15 dB or less	24 (57)	25 (73)	49 (64)
Mild hearing loss: threshold 16–40 dB			
8 kHz only	9 (21)	5 (15)	14 (18)
0.5–8 kHz	8 (19)	3 (9)	11 (14)
Moderate hearing loss: threshold above 40 dB	1 (2)	1 (3)	2 (3)
(B) No of children tested			
Normal hearing: threshold 15 dB or less	13 (62)	11 (65)	24 (63)
Mild hearing loss: threshold 16–40 dB			
8 kHz only	2 (10)	4 (23)	6 (16)
0.5–8 kHz	6 (28)	2 (11)	8 (21)

AC5 audiometer and TDH 39 headphones. Departmental normal values were obtained in 96 healthy children aged 8–10 years. Normal hearing was taken as threshold level of 15 dBHTL or better at all frequencies from 0.5–8.0 kHz.

(B) *Tympanometry and ASRT* using a Grayson Stadler GSI33 tympanometer. Normal middle ear pressure was taken as +50 to –150 daPa. Acoustic reflex thresholds were measured to 0.5, 1.2, and 4 kHz stimuli, presented ipsilaterally. Departmental normal values obtained in 36 healthy children aged 8–10 years were used. An abnormal response was recorded if the ASRT was greater than 105 dB at two or more adjacent frequencies when hearing was better than 60 dB. This is similar to the range established in adults.¹⁰

(C) *AEBRs* were recorded using a Medelec sensor system with click stimuli of 80 dB hearing level presented at 20 clicks/second and alternating polarity through standard TDH39 headphones. The average of 1024 sweeps was taken and latencies of waves I and V were analysed. These were considered abnormal if conduction time exceeded 2 SD from the age related departmental norms obtained in 36 healthy children aged 8–10 years.

Vestibular tests

The following procedures were carried out to assess vestibular function. Departmental normal values were obtained in 36 healthy children aged 8–10 years for all these tests.

(A) *ENG* was performed using a DC recorder to document: (i) spontaneous nystagmus with the slow phase velocity greater than 5°/sec; (ii) saccade and pursuit movements; and (iii) and optokinetic nystagmus.

(B) *Vestibular ocular reflex testing* was carried out with ENG recording of eye movements and: (i) clockwise and counterclockwise rotation in an AD9 rotating chair which was set in motion with an initial acceleration of 10°/sec and reached a final velocity of 120°/sec, followed by deceleration to 0°/sec in 1 sec. An abnormal response was taken as directional preponderance greater than 20%. (ii) Sinusoidal movement in an AD9 chair with frequency of 0.5 Hz and recording at maximal velocities rising from 9.4°/sec to 37.6°/sec. An abnormal response was taken as absent nystagmus at a velocity of 18.8°/sec and directional

preponderance greater than 20% in either direction.

(C) *Caloric testing* using the standard Hallpike and Fitzgerald technique with irrigation with water at 44° and 30° for 30 sec. Duration of response was recorded by direct vision, first with fixation, and then with abolition of fixation using Frenzel glasses to confirm normal enhancement of response. An abnormal response was taken as canal paresis greater than 15% or directional preponderance greater than 25%, that is, outside 2 SD for departmental norms.

STATISTICAL ANALYSIS

We have previously reported that outcome for intelligence at 3, 5, and 10 years was less satisfactory in the children with severe hypothyroidism,^{7–9} and one aim of the study was to ascertain whether severity of hypothyroidism at diagnosis also affected outcome for neurological function. Accordingly, the children were divided into two groups: 21 with pretreatment thyroxine concentrations of 40 nmol/l or below (severe) and 17 with initial thyroxine over 40 nmol/l (less severe).⁸ χ^2 Tests were used to assess the significance of differences between the groups. A *t* test was used to compare mean lengths in a standing broad jump test at 5 years in the children with and without abnormal ASRTs.

Results

CLINICAL ASSESSMENT

Otосcopy was normal in all but one child who had evidence of middle ear dysfunction. Of the 35 children tested, strabismus was present in four (all from the severely hypothyroid group) and in these cases ENG was made separately across each eye. Abnormal gait was found in 13 of the 31 children tested (table 2), seven on the Unterberger test, five on heel/toe walking, and one on both tests.

AUDIOMETRY AND TYMPANOMETRY

These tests were carried out in all the children. Three children had slightly negative pressures of –155 to –200 daPa on tympanometry; two had normal hearing and one had a mixed hearing loss.

Some sensorineural hearing loss was present

Table 2 Number (%) of abnormal test results for balance, vestibular function, ASRT, and AEBR in 38 children with congenital hypothyroidism. Values are numbers of children tested in each group with the percentage of abnormal results in parentheses

Type of test and result	Children with congenital hypothyroidism		
	Severe (n=21)	Less severe (n=17)	Total (n=38)
(A) Balance: clinical examination			
Abnormal	7/17 (41)	6/15 (40)	13/32 (41)
(B) Vestibular function tests			
Abnormal	9/15 (60)	3/14 (21)	12/29 (41)
(C) ASRT			
Abnormal	6/18 (33)	2/17 (18)	8/35 (23)
(D) AEBR (No of ears tested)			
Abnormal	1/40 (3)	1/32 (3)	2/72 (3)

in 18 children (table 1). Ten had loss at 8 kHz only, the thresholds ranging from 20–45 dB, and this was bilateral in three cases. In the children with an additional hearing loss at the other frequencies tested, thresholds were averaged over the range 0.5–8 kHz for each ear; the results classified by the number of ears tested are also shown in table 1. Only two ears (in two children) had average thresholds greater than 40 dB, three ears had average thresholds between 20–40 dB, and six average thresholds below 20 dB.

ASRT

ASRTs were measured in 35 children. Raised thresholds were found in eight (table 2), one child also having pathological delay. Five of these children had evidence of sensorineural hearing loss, four at 8 kHz only; in the other child hearing loss was mild and in none of these cases were the raised hearing thresholds sufficient to account for the abnormal ASRTs. Of the remaining three children with abnormal ASRTs, hearing was normal in the affected ear but one had tinnitus in the opposite ear.

AEBRS

These were recorded in response to ipsilateral stimulation in 36 children (table 2). The mean (SD) I–V latencies were 3.91 (0.34) ms and 3.93 (0.28) ms, respectively, for the right and left ears and two children were judged to have prolonged I–V latencies above the upper normal departmental limit of 4.37 ms. One had hearing loss in the opposite ear (balance was not tested), the other had normal hearing in both ears but impaired balance. Neither child had abnormal vestibular or ASRT results.

VESTIBULAR FUNCTION

Of the 29 children who completed all the tests, 12 had some abnormality (table 2). Four had absent caloric responses, seven had abnormal responses to rotational/sinusoidal movement, and one had abnormal responses to both tests.

RELATION TO SEVERITY OF HYPOTHYROIDISM

The results for the children with pretreatment thyroxine concentrations of 40 nmol/l or less, and those with values above 40 nmol/l are shown in tables 1 and 2. While there was a trend for the children with more severe hypothyroidism to show increased hearing loss, increased impairment of ASRT, and more frequent abnormalities on vestibular function tests, these differences were not of statistical significance.

RELATION TO TESTS OF MOTOR FUNCTION AT 5 YEARS

The eight children with one or more abnormal ASRT results did significantly less well on the standing broad jump test, one of the procedures used to assess motor function at 5 years; their mean (SD) jump length was 57.6 (12.4)

cm as opposed to 75.6 (17.3) cm achieved by the 25 children with normal ASRTs ($t=2.71$; $p<0.02$). No other significant associations were found between neuro-otological function and motor skills at 5 years.

Discussion

The results of this study indicate that children with congenital hypothyroidism have some impairment of hearing despite early treatment and that a significant number may have thresholds greater than 15 dB, a level of hearing which can be a significant handicap for spoken speech.¹¹ While we do not have matched controls for our study, the results can be compared with age related departmental norms and with those obtained in other studies in normal children. For example, Buren *et al* screened 172 normal 10 year olds and found that only 5% had hearing thresholds of 20 dB or greater at 8 kHz, as compared with 47% of the children in our study.¹²

Our results are similar to those of Francois *et al* in 42 children with early treated congenital hypothyroidism; 12 had sensorineural hearing loss of 20–50 dB at 8 kHz and two had mild bilateral hearing loss at conversational frequencies.⁴ Again, Vatovec *et al* tested hearing in 63 children with congenital hypothyroidism and found impaired hearing in nine.⁵

In comparison with earlier studies carried out before the introduction of screening for congenital hypothyroidism, the prevalence of impaired hearing appears unchanged. For example, Crifo *et al* found that over 50% of their subjects had some degree of sensorineural hearing impairment,² compared with 47% in our study and Debruyne *et al* found bilateral sensorineural hearing impairment in 20% of their cases,³ compared with 23% of patients in our study. However, unlike these earlier studies, none of our cases showed evidence of severely impaired hearing with thresholds of 50 dB or greater in the better ear. Only two (5%) children had bilateral hearing loss with a better ear threshold of 20–40 dB, one of whom needed amplification. This compares with an incidence of 13% with an average threshold worse than 20 dB in the better ear and 9% with thresholds greater than 41 dB reported by Debruyne *et al*.³ These results, together with our own findings, suggest that the effects of congenital hypothyroidism on hearing can be largely prevented by early treatment, even though relatively minor degrees of hearing impairment which are of little clinical consequence can still be documented.

In the present study ASRT and AEBRs were carried out to identify any abnormalities of the auditory/neural pathways. Abnormalities of ASRT can result from pathology affecting any part of the reflex system and Lutman showed that middle ear disorders with a 20 dB air-bone gap account for about half the abnormalities of ASRT.¹³ However, in our study the only child with any air-bone gap had normal ASRTs and AEBRs and in none of the children with raised or absent ASRTs could this be explained by hearing impairment. Abnormal ASRT and

decay are seen with neural lesions and eight (23%) of our patients showed this pattern of abnormality which is consistent with neural pathology. Dussault and Hébert studied evoked potentials in 34 children with early treated congenital hypothyroidism and reported that seven showed a prolonged interval between waves I-V.¹⁴ They considered that their findings could reflect high frequency hearing loss but as the subjects were neonates the actual hearing thresholds were unknown. Their results are generally similar to our own findings of abnormal evoked responses in two of the 36 children tested.

Sato *et al* investigated vestibular function in 13 patients with congenital hypothyroidism and found that five had peripheral vestibular disorders and five had cerebellovestibular disorders.⁶ Our results indicate that vestibular function may still be impaired in congenital hypothyroidism despite early treatment, in that almost half the children tested showed an abnormality. In all cases this was a peripheral vestibular abnormality.

Impaired coordination was very common in children with congenital hypothyroidism born before introduction of screening.¹⁵ In the present subjects, Fuggle *et al* reported that motor coordination was impaired at the age of 5 years despite early treatment.⁷ We were able to demonstrate that the subjects with abnormal ASRTs performed significantly less well on a test of motor function carried out at 5 years of age (the standing broad jump), suggesting that impaired motor performance may have been related to abnormal development of neural pathways.

In conclusion, we have shown that minor impairment of hearing is common in children with congenital hypothyroidism despite early treatment, although the severity of hearing loss is much less when compared with studies carried out before introduction of screening. In addition, we have shown abnormalities of peripheral audiovestibular function in several of

our patients; the abnormal ASRTs correlated with previous impairment of gross motor performance. The study provides further evidence that neurological impairment of some degree persists in subjects with congenital hypothyroidism despite early treatment.

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